DOCKET NO.: ADOL-0762 **Application No.:** Not yet assigned

Preliminary Amendment - First Action Not Yet Received

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1 to 19. (canceled)

20. (Added) A compound of the formula IIIA or a pharmaceutically acceptable salt thereof:

$$N_{Ar}$$
 N_{Ar}
 N_{Ar}

wherein:

n is 1 to 3;

 R_1 and R_2 are independently CH_3 or together form - $(CH_2)_m$ -, - $CH_2CH(OR)(CH_2)_2$ -, - $CH_2CH(F)(CH_2)_2$ -, - $(CH_2)_2O(CH_2)_2$ - or - $(CH_2)_2CH=CHCH_2$ -;

R is H, alkyl, acyl or aroyl;

Ar is mono- or di-substituted phenyl, wherein said substituents are selected from the group consisting of halogen, OCH₃, OH, SO₂CH₃, CF₃, NH₂, alkyl, CN, unsubstituted and substituted sulfamoyl groups;

Ar may also be substituted with NH(CH₂)_uCO₂R',

 $NH(CH_2)_u(CH=CH)_u(CH_2)CO_2R',\ NHCO(CH_2)_u(CH=CH)_u(CH_2)_uCO_2R',\ NHP(O)(OBn)_2,\\ NHP(O)(OR')_2,\ (CH_2)_uNHSO_2CH_3,\ (CH_2)_uNHC(S)NHCH(CO_2R')(CH_2)_uCO_2R',\ CONHOH,\\ or\ (CH_2)_uCONHOH;$

or Ar is substituted with

$$+ \underbrace{N}_{V} \underbrace{NHR_{6}}_{VX_{8}} \qquad \text{or} \qquad -0 \underbrace{NHR_{6}}_{VX_{8}}$$

R₆ is H or Ac;

R₇ is NH(CH₂)_vCO₂H, NH(CH₂)_vCH(NH₂)(CO₂H), NHCH(CO₂H)(CH₂)_vNH₂, NH(CH₂)_vSO₃H, NH(CH₂)_vPO₃H, NH(CH₂)_vNHC(NH)NH₂, or NHCH(CO₂H)(CH₂)_vCO₂H; R' is H or lower alkyl;

Application No.: Not yet assigned

Preliminary Amendment - First Action Not Yet Received

X₇ is H, halogen, OH, OCH₃, CF₃, NO₂, NH₂, amino substituted with acyl, carbamate, alkyl or aryl sulfonates, or COR";

R" is OH, amide, alkoxy, aryloxy or heteroaryloxy;

 X_8 is CO_2H , $NHSO_2CH_3$, $NHP(O)(OBn)_2$, $NHP(O)(OH)_2$, $OP(O)(OBn)_2$, or $OP(O)(OH)_2$;

m is 4 to 8;

u is 0 to 5; and

v is 1 to 20.

- 21. (Added) A compound which is selected from the group consisting of N-[(4-Trifluoromethylphenyl)-N-methyl-{[1S-1-phenyl-2-[1-pyrrolidinyl)]ethyl}-acetamido]glycine hydrochloride;
- 2-(3,4-Dichlorophenyl)-N-methyl-N-[(1R, S)-1-(3-sulfamidophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide hydrochloride;
- 2-(4-Trifluoromethylphenyl)-N-methyl-N-{[1S]-1-[3-[(methylsulfonyl)amino]-phenyl]-2-[1-pyrrolidinyl]ethyl}acetamide hydrochloride;
- 2-(4-Methanesulfonylphenyl)-N-methyl-N-{[1S]-1-[3-[(methylsulfonyl)amino]-phenyl]-2-[1-pyrrolidinyl]ethyl} acetamide methanesulfonate;
- 2-(3,4-Dichlorophenyl)-N-methyl-N-{[1S]-1-[3-[(methylsulfonyl)amino]phenyl]-2-[1-pyrrolidinyl]ethyl}acetamide hydrochloride;
- 2-(3,4-Dichlorophenyl)-N-methyl-N-[(1S)-1-[3-(diethyl phosphoryl)amino]phenyl)-2-(1-pyrrolidinyl)ethyl]acetamide hydrochloride;
- 2-(3,4-Dichlorophenyl)-N-methyl-N-[(1S)-1-[3-[(4-oxo-butenoate)]amino]phenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;
- 2-(3,4-Dichlorophenyl)-N-methyl-N-{(1S)-1-[3-(3-(((iso-butoxycarbonyl)-methyl)aminocarbonyl)propionamdo)phenyl]-2-(1-pyrrolidinyl)ethyl} acetamide hydrochloride;
- 2-(3,4-Dichlorophenyl)-N-methyl-N-{(1R, S)-1-[3-(3-(((hydroxycarbonyl)-methyl)aminocarbonyl)propionamido)phenyl]-2-(1-pyrrolidinyl)ethyl} acetamide hydrochloride;

Application No.: Not yet assigned

- 2-[(2-N-Phenylsulfonamido)phenyl)]-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide methane sulfonate;
- 2-[3-(N-Methylsulfamoyl)-4-chlorophenyl]-N-methyl-N-{[1S]-1-phenyl-2-[1-pyrrolidinyl]ethyl}acetamide hydrochloride;
- 2-(3-Sulfamoyl-4-chlorophenyl)-N-methyl-N-{[1S]-1-phenyl-2-[1-pyrrolidinyl]-ethyl} acetamide methanesulfonate;
- 2-(3-Sulfamoyl-4-chlorophenyl)-N-methyl-N-{[1S]-1-[3-[(methylsulfonyl)amino]-phenyl]-2-[1-pyrrolidinyl]ethyl} acetamide methanesulfonate;
- 2-[3-(N-Methylsulfamoyl)-4-fluorophenyl]-N-methyl-N-{[1S]-1-phenyl-2-[1-pyrrolidinyl]ethyl}acetamide hydrochloride;
- 2-[2&4-(N-Methylsulfamoyl)phenyl]-N-methyl-N-[(1S)-1-phenyl-2-[1-pyrrolidinyl)-ethyl]acetamide hydrochloride;
- 3-(N-Methylsulfamoyl)phenyl-N-methyl-N-[(1S)-phenyl-2-(1-pyrrolidinyl)ethyl]-acetamide hydrochloride;
- 2-[N-Methylsulfamoyl)-4-bromophenyl]-N-methyl-N-[(1S)-1-phenyl-2-[1-pyrrolidinyl]ethyl acetamide hydochloride;
- 2-[2&4-(N-Methylsulfamoyl)phenyl]-N-methyl-N-{[1S]-1-phenyl-2-[1-(3S)-3-hydroxypyrrolidinyl]ethyl}acetamide hydrochloride;
- 2-[2-Methoxy-3-(N-methylsulfamoyl)phenyl]-N-methyl-N-{[1S]-1-phenyl-2-(1-pyrrolidinyl)ethyl}acetamide hydrochloride;
- (Z)-4-[2-(2-Aminophenyl)-N-methyl-N-[(1S)-1-phenyl)-2-[1-(3S)-3-hydroxypyrrolidinyl]ethyl]acetamido]-4-oxo-2-butenoic acid;
- (Z)-4-[2-(2-Amino-4,5-dichlorophenyl)-N-methyl-N-[(1S)-1-phenyl)-2-[1-pyrrolidinyl]ethyl]acetamido]-4-oxo-butanoic acid;
- (Z)-4-[2-(2-Amino-4,5-dichlorophenyl)-N-methyl-N-[(1S)-1-phenyl)-2-[1-pyrrolidinyl]ethyl]acetamido]-4-oxo-2-butenoic acid;
- (E) Ethyl 4-[2-(2-amino-4,5-dichorophenyl)-N-methyl-N-[(1S)-1-phenyl)-2-[1-pyrrolidinyl]ethyl]acetamido]-4-oxo-2-butenoate hydrochloride;

Application No.: Not yet assigned

- (Z)-4-[2-(2-Amino-4-trifluoromethylphenyl)-N-methyl-N-[(1S)-1-phenyl)-2-[1-pyrrolidinyl]ethyl]acetamido]-4-oxo-2-butenoic acid;
- (Z)-4-[2-(2-Aminophenyl)-N-methyl-N-[(1S)-1-phenyl)-2-[1-pyrrolidinyl]-ethyl]acetamido]-4-oxo-2-butenoic acid hemimaleate;
- 2-(N,N-Bisacetic acid-2-amino- α , α , α ,-trifluoro-4-tolyl)-N-methyl-N-[(1S)-1- phenyl-2-(1-pyrrolidinyl)ethyl]acetamide hydrochloride;
- 3-[2-N-Methylsulfonamido)phenyl]-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)-ethyl]acetamide hydrochloride;
- 2-(O-Butylacetate)phenyl-N-methyl-N-[(1S)-1-phenyl-2-[1-pyrrolidinyl]ethyl acetamide hydrochloride;
 - 2-[Phenoxy-acetyl]methylamino(1-pyrrolidinyl) ethyl]acetamide]hydrochloride;
- 2-[4-Trifluoromethylphenyl]-N-methyl-N-{[1S]-1-phenyl-2-[1-(3S)-3-hydroxy-pyrrolidinyl]ethyl}acetamide hydrochloride;
- 2-(2-Pyridyl)-N-methyl-N-{[1S]-1-phenyl-2-[1-(3S)-3-hydroxypyrrolidinyl]ethyl}-acetamide dihydrochloride;
- 2-(5-Bromo-3-pyridyl)-N-methyl-N-[(1S)-1-phenyl-2-pyrrolidinyl ethyl]acetamide hydrochloride;
- 2-(5-Bromo-3-pyridyl)-N-methyl-N-{[1S]-1-phenyl-2-[1-(3S)-3-hydroxy-pyrrolidinyl]ethyl}acetamide hydrochloride;
- 2-(9-Anthracenyl)-N-methyl-N-{[1S]-1-phenyl-2-(1-pyrrolidinyl)ethyl}acetamide hydrochloride;
- 2-(2-Carboxyphenyl)-N-methyl-N-{[1S]-1-phenyl-2-(1-pyrrolidinyldethyl}acetamide hydrochloride;
- [2-(2-Phenyl)-N-methyl-N-{[1S]-1-phenyl-2-(1-pyrrolidinyl)ethyl}acetamido]-2-oxoglycine hydrochloride;
- Methyl N-[2-(2-phenyl)-N-methyl-N-{[1S]-1-phenyl-2-(1-pyrrolidinyl)ethyl}-acetamido]-2-oxo-glycinate hydrochloride;

Application No.: Not yet assigned

- 2-(3,4-Dihydroxyphenyl)-N-methyl-N-{[1S]-1-phenyl-2-(1-pyrrolidinyl)ethyl}-acetamide hydrochloride;
- 2-(3,4-Dimethoxyphenyl)-N-methyl-N-{[1S]-phenyl-2-(1-pyrrolidinyl)ethyl}-acetamide hydrochloride;
- 2-(2-Methanesulfonamidophenyl-N-methyl-N-[(1S)-1-(3-methanesulfonamidophenyl-2-(1-pyrrolidinyl)ethyl]acetamide hydrochloride;
- 2-(2-Iso-butyramidophenyl)-N-methyl-N-[(1S)-1-(3-isobutyramido-phenyl)-2-(1-pyrrolidinyl)ethyl]acetamide methanesulfonic acid salt;
- 4-[4-N-Methylsulfonamido-phenyl]-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)-ethyl] acetamide hydrochloride;
- 2-(3,4-Dichlorocinnamyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)-ethyl]acetamide hydrochloride;
- 2-(2-Nitrocinnamyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl) ethyl]acetamide hydrochloride;
- (R,S)-1-[2-(Methanesulfonylamino)-phenyl-N-methylacetamido]-1-(3-methoxy-phenyl)-2-(1-pyrrolidino)-ethane, methanesulfonic acid salt;
- (R,S)-1-[2-(Methanesulfonylamino)-phenyl-N-methylacetamido]-1-(3-hydroxy-phenyl)-2-(1-pyrrolidino)ethane, methanesulfonic acid salt;
- 2-(3-Indolyl)-N-methyl-N-[(1S)-1-phenyl-2-[(3S)-1-pyrrolidin-3-ol]ethyl]-acetamide hydrochloride;
- 2-(2-N-Benzyl-2-N-methylsulfamoyl-3,4-dimethoxyphenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide hydrochloride;
- 2-(N-Methylsulfonamido-2-aminophenyl)-N-methyl-N-[(1R)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide methane sulfonate;
- (R,S)-1-(4-Trifluoromethylphenyl-N-methylacetamido)-1-(3-methoxyphenyl)-2-(1-pyrrolidino)-ethane, methanesulfonic acid salt;
- (R,S)-1-(4-Trifluoromethylphenyl-N-methylacetamido)-1-(3-hydroxyphenyl)-2-(1-pyrrolidino)-ethane, methanesulfonic acid salt;

Application No.: Not yet assigned

Preliminary Amendment - First Action Not Yet Received

2-Fluorophenyl-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]-acetamide hydrochloride;

PATENT

- 4-Fluorophenyl-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide hydrochloride; and
- (E)-4-[2-(2-Amino-4,5-dichlorophenyl)-N-methyl-N-[(1S)-1-phenyl)-2-[1-pyrrolidinyl]ethyl]acetamido]-4-oxo-2-butenoic acid hydrochloride.
- 22. (Added) A pharmaceutical composition comprising a compound of claim 20 in a pharmaceutically acceptable carrier.
- 23. (Added) A pharmaceutical composition comprising a compound of claim 21 in a pharmaceutically acceptable carrier.
- 24. (Added) A method of treating hyperalgesia in a patient comprising administereing to said patient an effective amount of a compound of claim 20.
- 25. (Added) A method of treating hyperalgesia in a patient comprising administereing to said patient an effective amount of a compound of claim 21.
- 26. (Added) A method of treating hyperalgesia in a patient comprising administereing to said patient an effective amount of the pharmaceutical composition of claim 22.
- 27. (Added) A method of treating hyperalgesia in a patient comprising administereing to said patient an effective amount of the pharmaceutical composition of claim 23.
- 28. (Added) A pharmaceutical composition comprising a compound of claim 20 and an antibiotic, antiviral, antifungal, anti-inflammatory agent, or a mixture thereof in a pharmaceutically acceptable carrier.

DOCKET NO.: ADOL-0762 **Application No.:** Not yet assigned

Preliminary Amendment - First Action Not Yet Received

- 29. (Added) A pharmaceutical composition comprising a compound of claim 21 and an antibiotic, antiviral, antifungal, anti-inflammatory agent, or a mixture thereof in a pharmaceutically acceptable carrier.
- 30. (Added) A compound of the formula IVA or a pharmaceutically acceptable salt thereof:

$$R_4$$
 R_3 R_1 R_2 R_1 R_2 R_1 R_2

wherein:

n is 1 to 3;

 R_1 and R_2 are independently CH_3 or together form - $(CH_2)_m$ -, - $CH_2CH(OR)(CH_2)_2$ -, - $CH_2CH(F)(CH_2)_2$ -, - $(CH_2)_2O(CH_2)_2$ - or - $(CH_2)_2CH=CHCH_2$ -;

R is H, alkyl, acyl or aroyl;

 R_3 and R_4 are independently H, OCH₃, alkyl or -O(CH₂)₂-;

each X_9 is independently selected from the group consisting of halogen, CF_3 , OH, OCH₃, $SO_2NH(CH_2)_qCH_3$, $NH(CH_2)_qCO_2R'$, $NH(CH_2)_q(CH=CH)_q(CH_2)_qCO_2R'$, $NH(CH_2)_q(CH=CH)_q(CH_2)_qCO_2R'$, $NHCO(CH_2)_q(CH=CH)_q(CH_2)_qCO_2R'$, and $NHCO(CH_2)_q(CH=CH)_q(CH_2)_qCO_2R'$;

R' is OH, lower alkyl, aryl ester or aryl amide;

q is 0 to 20; and

y is 1 to 4.

- 31. (Added) A compound which is selected from the group consisting of
- (Z)-4-[2-((±)-trans-2-Amino-4,5-dichloro-N-methyl-N-[2-(1-pyrrolidinyl)-cyclohexyl]phenylaetamido)]-4-oxo-2-butenoic acid;
- (Z)-4-[2-((±)-trans-2-Amino-4-trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)-cyclohexyl]-phenylaetamido)]-4-oxo-2-butenoic acid;

Application No.: Not yet assigned

- (±)-trans-2-N-Methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-pyridylacetamide dihydrochloride;
- (±)-trans-3-N-Methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-5-bromo-pyridylacetamide hydrochloride;
- (±)-trans-3,5-Di-Trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide hydrochloride;
- (±)-trans-3-N-Methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-(trans-3-furyl)acetamide hydrochloride;
- (±)-trans-2-Methoxy-3-methylsulfamoyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide hydrochloride;
- (±)-trans-3-N-Methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]indoleacetamide hydrochloride;
- (±)-trans-4-Fluoro-3-methylsulfamoyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide hydrochloride;
- N-[1S,2S-trans-4-Trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamido]glycine hydrochloride; and
- N-[1R,2R-trans-4-Trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamido]glycine hydrochloride.
- 32. (Added) A pharmaceutical composition comprising a compound of claim 30 in a pharmaceutically acceptable carrier.
- 33. (Added) A pharmaceutical composition comprising a compound of claim 31 in a pharmaceutically acceptable carrier.
- 34. (Added) A method of treating hyperalgesia in a patient comprising administering to said patient an effective amount of a compound of claim 30.

DOCKET NO.: ADOL-0762 PATENT

Application No.: Not yet assigned

Preliminary Amendment - First Action Not Yet Received

35. (Added) A method of treating hyperalgesia in a patient comprising administering to said patient an effective amount of a compound of claim 31.

- 36. (Added) A method of treating hyperalgesia in a patient comprising administering to said patient an effective amount of the pharmaceutical composition of claim 32.
- 37. (Added) A method of treating hyperalgesia in a patient comprising administering to said patient an effective amount of the pharmaceutical composition of claim 33.
- 38. (Added) A pharmaceutical composition comprising a compound of claim 30 and an antibiotic, antiviral, antifungal, anti-inflammatory agent, or a mixture thereof in a pharmaceutically acceptable carrier.
- 39. (Added) A pharmaceutical composition comprising a compound of claim 31 and an antibiotic, antiviral, antifungal, anti-inflammatory agent, or a mixture thereof in a pharmaceutically acceptable carrier.